Table 1. Unique polymorphisms in the HIV-1 sequences isolated from patient 671 that are present in the whole period of infection.

| in the whole period of infection. |  |  |                  |  |  |  |
|-----------------------------------|--|--|------------------|--|--|--|
| Region in HIV-1                   |  | Polymorphism. (amino acid sequences)   | Consensus B      |  |  |  |
| Gag                               | 118<br>464<br>541                      | 3 aa (QAE) insertion<br>10 aa (QSRPEPTAPP) duplication<br>stopcodon <sup>2</sup> | s                |  |  |  |
| Pol                               | 196 (RT 41)<br>370 (RT 215)<br>621-624 | L<br>Y³, D<br>IPIK   | M<br>T<br>VSLN/T |  |  |  |
| Nef                               | 48-49                                  | 2 aa deletion*   |                  |  |  |  |
| Env                               | 423-425                                | LYK  | QFG              |  |  |  |

- amino acid numbering is according to the numbering of the amino acid sequences of the HIV-1 consensus B sequences of the different HIV-1 genes in the Los Alamos database (http:/hiv-web.lanl.gov, Human Retroviruses and AIDS 1999: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences. Kuiken CL, Foley B, Hahn B, Korber B, McCutchan F, Marx PA, Mellors JW, Mullins JI, Sodroski J, and Wolinksy S, Eds. Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM)
  - 2. Two amino acids before the normal stopcodon of gag.
  - 3. AZT resistance conferring mutations
  - 4. Polymorphism previously described by Alexander et al. (2000), J. Virol 74.

Table 2. Genotypic characteristics of the HIV-1 sequences at early versus late time point isolations in the infection

| time point isolations in the injection |   |   |                                      |  |  |  |
|--|---|---|--------------------------------------|--|--|--|
| Region in HIV-1                        | aa number'  | Early isolate                                 | Late isolate                         |  |  |  |
|  |   |   |                                      |  |  |  |
|  | Partie of the contract of the | 1. "益果等效物"                                    |                                      |  |  |  |
| 事情的"大学"。                               | 1244 than ™a dv.a.  | <u> 17                                   </u> | <b>经验证证据</b> 医皮肤 医                   |  |  |  |
| Pol (p66/p51)                          | 60  | $\mathbf{v}$                                  | 1                                    |  |  |  |
|  | 135   | I   | T                                    |  |  |  |
|  | 215   | Y<br>I  | T<br>D                               |  |  |  |
| t e                                    | 593   | I   | V                                    |  |  |  |
|  |   |   |                                      |  |  |  |
| Rev                                    | 51  | Q<br>S  | R                                    |  |  |  |
| 1                                      | 54  | S   | A                                    |  |  |  |
|  |   |   |                                      |  |  |  |
| Nef                                    | 9   | S   | K                                    |  |  |  |
|  | 113   | I   | V                                    |  |  |  |
| Í .                                    |   |   |                                      |  |  |  |
| Tat                                    | 52  | W   | R                                    |  |  |  |
|  | 100   | $\mathbf{v}$                                  | G                                    |  |  |  |
|  |   |   |                                      |  |  |  |
|  | 43  | G   | E                                    |  |  |  |
| 1                                      | 117   | N<br>E<br>K                                   | D                                    |  |  |  |
|  | 159   | E   | A                                    |  |  |  |
|  | 187   | K   | S                                    |  |  |  |
| Env                                    | 193   | ${f v}$                                       | D<br>A<br>S<br>I                     |  |  |  |
| gp120                                  | 201   | R   | K                                    |  |  |  |
| Ðr                                     | 207   | R<br>Q<br>R<br>T                              | K                                    |  |  |  |
|  | 243   | Ř   | G                                    |  |  |  |
| ]                                      | 343   | T   | Á                                    |  |  |  |
| 1                                      | 350   | R   | K                                    |  |  |  |
|  | 416   | I   | G                                    |  |  |  |
|  | 439   | P   | Š                                    |  |  |  |
|  | 456   | P<br>G<br>S                                   | Ř                                    |  |  |  |
| gp41                                   | 505   | S   | K<br>G<br>A<br>K<br>G<br>S<br>R<br>P |  |  |  |
| er                                     |   |   |                                      |  |  |  |

 amino acid numbering is according to the numbering of the aminoacid sequences of the HIV-1 consensus B sequences of the different HIV-1 genes in the Los Alamos database (<a href="http://hiv-web.lanl.gov">http://hiv-web.lanl.gov</a>, Human Retroviruses and AIDS 1999: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences. Kuiken CL, Foley B, Hahn B, Korber B, McCutchan F, Marx PA, Mellors JW, Mullins JI, Sodroski J, and Wolinksy S, Eds. Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM))

5

Table 3. Genotypic characteristics of the HIV-1 sequences isolated late in the infection that replicate fast versus slow in culture

|                 | infection that replicate fast versus slow in culture |             |                       |  |  |  |  |
|-----------------|--|-------------|-----------------------|--|--|--|--|
| Region in HIV-1 | aa number'   | Fast        | Slow                  |  |  |  |  |
|                 |  | réplication | replication           |  |  |  |  |
|                 | 4. 特别:我说   |             |                       |  |  |  |  |
| Pol (p66/p51)   | 40   | l E         | A                     |  |  |  |  |
|                 | 841  | G           | D                     |  |  |  |  |
| Rev             | 18   | L           | 1                     |  |  |  |  |
|                 | 21   | F           | Y                     |  |  |  |  |
|                 | 84   | G           | D                     |  |  |  |  |
| Gag             | 385  | N           | S<br>S                |  |  |  |  |
|                 | 538  | N           | S                     |  |  |  |  |
| Vif             | 9  | G           | Ι                     |  |  |  |  |
|                 | 17<br>61   | H<br>D      | Y                     |  |  |  |  |
|                 | 61   | D           | Y<br>E<br>S<br>Q      |  |  |  |  |
|                 | 130  | R           | S                     |  |  |  |  |
|                 | 159  | K           | Q                     |  |  |  |  |
| Vpr             | 41   | G           | V                     |  |  |  |  |
| Env             | 4  | R           | K                     |  |  |  |  |
|                 | 31   | M           | T                     |  |  |  |  |
| gp120           | 44   | ĸ           | Ň                     |  |  |  |  |
|                 | 193  | T           | Ā                     |  |  |  |  |
|                 | 329  | E           | D                     |  |  |  |  |
| gp41            | 530  | E<br>E      | <b>A</b>              |  |  |  |  |
| 9r ·            | 736  | N           | E                     |  |  |  |  |
|                 | 752  | N           | S                     |  |  |  |  |
|                 | 845  | G<br>V      | E                     |  |  |  |  |
|                 | 891  |             | E<br>S<br>E<br>I<br>F |  |  |  |  |
|                 | 937  | L           | F                     |  |  |  |  |

 amino acid numbering is according to the numbering of the aminoacid sequences of the HIV-1 consensus B sequences of the different HIV-1 genes in the Los Alamos database (<a href="http://hiv-web.lanl.gov">http://hiv-web.lanl.gov</a>, Human Retroviruses and AIDS 1999: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences. Kuiken CL, Foley B, Hahn B, Korber B, McCutchan F, Marx PA, Mellors JW, Mullins JI, Sodroski J, and Wolinksy S, Eds. Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM))

10

Table 4. Genotypic characteristics of the HIV-1 sequences isolated early in the infection that replicate fast versus slow in culture

| Region in HIV-1 | aa number'             | Fast replication | Slow<br>replication |  |  |  |
|-----------------|------------------------|------------------|---------------------|--|--|--|
|                 |                        |                  |                     |  |  |  |
| Rev             | 52                     | E                | Q                   |  |  |  |
|                 | 111                    | E                | D                   |  |  |  |
| Nef             | 101                    | L                | F                   |  |  |  |
|                 | 197                    | H                | Q                   |  |  |  |
|                 | 207                    | F                | Y                   |  |  |  |
| Tat             | 11                     | C                | W                   |  |  |  |
|                 | 64                     | N                | T                   |  |  |  |
|                 | 85                     | E                | K                   |  |  |  |
| Env<br>gp120    | 4<br>171<br>172<br>392 | K<br>I<br>T      | R<br>T<br>S         |  |  |  |
| gp41            | 396                    | R                | I                   |  |  |  |
|                 | 860                    | S                | G                   |  |  |  |
|                 | 910                    | D                | E                   |  |  |  |
|                 | 926                    | S                | I                   |  |  |  |

 amino acid numbering is according to the numbering of the aminoacid sequences of the HIV-1 consensus B sequences of the different HIV-1 genes in the Los Alamos database (<a href="http://hiv-web.lanl.gov">http://hiv-web.lanl.gov</a>, Human Retroviruses and AIDS 1999: A Compilation and Analysis of Nucleic Acid and Amino Acid Sequences. Kuiken CL, Foley B, Hahn B, Korber B, McCutchan F, Marx PA, Mellors JW, Mullins JI, Sodroski J, and Wolinksy S, Eds. Theoretical Biology and Biophysics Group, Los Alamos National Laboratory, Los Alamos, NM))

10

15

## **CLAIMS**

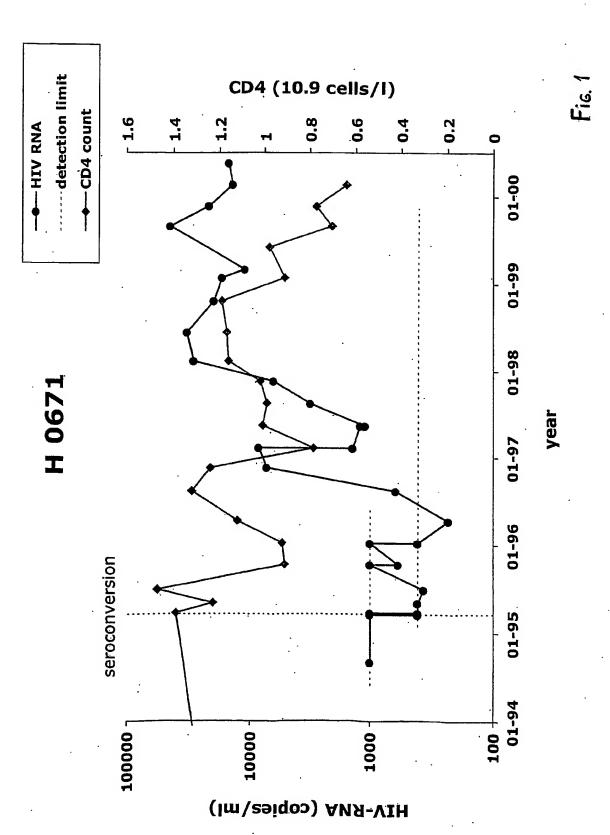
- 1. An isolated human immunodeficiency virus, comprising at least one non revertant mutation capable of delaying or diminishing the pathological behavior of said immunodeficiency virus when compared to a human immunodeficiency virus not having at least one such a mutation.
- 5 2. A virus according to claim 1, comprising at least one amino acid sequence as described in table 1 or 2.
  - 3. A virus according to claim 1, comprising at least one amino acid sequence as described in table 1.
- 4. A virus according to claim 2 or 3, which comprises at least one substitution
   amino acid in said amino acid sequence.
  - 5. A method for obtaining a virus according to anyone of claims 1-4, comprising providing a wild type human immunodeficiency virus with at least one non revertant mutation capable of delaying or diminishing the pathological behavior of said immunodeficiency virus when compared to a human immunodeficiecy virus not having at least one such a mutation.
  - 6. A method for obtaining a virus according to claim 1-4, comprising -collecting a certain number of strains,
  - -sequencing at least part of said strains,
  - -comparing obtained sequences with sequences of virus according to claim 1-4,
- -isolating strains comprising sequence similarities to a virus according to claim 1-4.
  - 7. A method according to claim 6, wherein said strain is amplified before sequencing.
  - 8. A virus obtainable by a method according to claim 6 or 7.
- 25 9. A virus according to anyone of claims 1-4 or 8 for use as a vaccine.
  - 10. Use of a virus according to anyone of claims 1-4 or 8 for the preparation of a vaccine.

WO 02/20571 PCT/EP01/10244

24

- 11. Use of a virus according to anyone of claims 1-4 or 8 for the preparation of a vaccine for Aids.
- 12. A vaccine comprising virus according to anyone of claims 1-4 or 8.
- 13. A method for identifying virus according to anyone of claims 1-4 or 8 in an individual comprising:
  - collecting a sample comprising virus or parts thereof from said individual,
  - -detecting strains comprising sequence similarities to a virus according to claim 1-4 or 8.
- 14. A method according to claim 13, wherein said virus is collected by isolatingperipheral blood monocytic cells from said individual.
  - 15. A method according to claim 13 or 14, wherein said sequence similarities are detected by sequencing.
  - 16. A method according to claim 13 or 14, wherein said sequence similarities are detected by hybridization with probes comprising at least one sequence of virus according to anyone of claims 1-4 or 8.
    - 17. A method for, at least in part, prophylaxis of Aids, comprising administering a vaccine according to claim 12 to an individual.

15



Isolateu 1º moment.

